REMARKS

The October 15, 2008 Official Action and the references cited therein have been carefully reviewed. In view of the amendments presented herewith and the following remarks, favorable reconsideration and allowance of this application are respectfully requested. The present remarks and amendments are being filed as part of the submission required under 37 C.F.R. §1.114, in connection with the Request for Continued Examination, which is submitted concurrently herewith.

At the outset, a shortened statutory response period of three (3) months was set forth in the October 15, 2008 Official Action. Therefore, the initial due date for response is January 15, 2009.

The Examiner has rejected claims 38, 39, 41-47, 53, and 54 for allegedly failing to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph.

The foregoing rejection constitutes all of the grounds set forth in the October 15, 2008 Official Action for refusing the present application.

In accordance with the instant amendment, claims 55 and 56 have been added. Support for new claims 55 and 56 can be found throughout the application including, for example, in original claim 47. No new matter has been introduced into this application by reason of any of the amendments presented herewith.

In view of the present amendment and the reasons set forth in this response, Applicants respectfully submit that the 35 U.S.C. §112, first paragraph rejection of claims 38, 39, 41-47, 53, and 54, as set forth in the October 15, 2008 Official Action, cannot be maintained. This ground of rejection is, therefore, respectfully traversed.

CLAIMS 38, 39, 41-47, 53, AND 54 SATISFY THE ENABLEMENT REQUIREMENT OF 35 U.S.C. §112, FIRST PARAGRAPH

The Examiner has rejected claims 38, 39, 41-47, 53 and 54 for allegedly failing to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph. It is the Examiner's position that while the specification is enabling for the treatment of breast cancer, the specification does not reasonably provide enablement for the treatment of other cancers. Applicants continue to respectfully disagree with the Examiner's position for the reasons of record and those set forth below.

At the outset, the Examiner notes that the elected IDO inhibitor species are 1-methyl-tryptophan (1MT) and methyl-TH-Trp and the elected chemotherapeutic compound species is cisplatin.

The Examiner then argues that the data provided in Hou et al. (Cancer Res. (2007) 67:792-801), submitted with the last Official Action response, does not lend support to the instantly claimed invention. Applicants respectfully disagree. Figure 1A of Hou et al. clearly demonstrates that the administration of 1MT and the chemotherapeutic agent cyclophosphamide (black squares) resulted in a dramatic reduction in the volume of a melanoma tumor. As stated hereinabove, cyclophosphamide is not the elected species of chemotherapeutic compound. However, cyclophosphamide and cisplatin are in the same class of chemotherapeutic compound. Indeed, both cyclophosphamide and cisplatin are DNA crosslinkers which cross link guanines within the DNA. This crosslinking ultimately results in apoptosis (cell death) in the cancer cells. Inasmuch as cisplatin and cyclophosphamide have a similar mechanism of action, a skilled artisan would anticipate that the ability of one of the chemotherapeutic compounds to treat cancer would be indicative of the other compound's ability.

Furthermore, Figure 1A of Hou et al. demonstrates that the administration of either 1MT alone or cyclophosphamide

alone did not yield a significant reduction in melanoma tumor volume 4 weeks after administration. However, the co-administration of 1MT and cyclophosphamide led to a dramatic decrease in tumor volume compared to controls and the administration of either compound individually (P value of < 0.05). The Examiner states at page 3 of the Official Action that "1MT has no effect when administered alone, lending no support to the instantly claimed treatment against other tumor types." The Examiner's conclusion, however, is incorrect. Indeed, the instant claims are drawn to the co-administration of ***both*** an IDO inhibitor and a chemotherapeutic compound. Significantly, the instant application clearly demonstrates that the administration of 1-MT alone does not reduce breast tumor volume. Indeed, Figure 5 of the instant application demonstrates that the breast tumor ***increased*** in volume after a two week course of 1MT. Similarly, the breast tumor volume is shown to ***increase*** when either cisplatin or cyclophosphamide is administered individually over a two week course. In complete contrast, Figure 5 of the instant application shows surprising finding that the ***co***-administration of either 1MT and cisplatin or 1MT and cyclophosphamide led to a dramatic ***reduction*** in breast tumor volume over a two week course. Similarly, at page 4 of the Official Action, the Examiner argues that "methyl-TH-DL-Trp has no effect when administered alone, lending no support to the efficacy of the instantly examined treatment against other tumor types." Again the Examiner's conclusion is incorrect for the same reasons as argued for 1MT above.

The similarity between the data provided in the instant application and the data provided in Hou et al. is clear. Both demonstrate that the administration of only an IDO inhibitor such as 1MT or only a chemotherapeutic agent such as cisplatin or cyclophosphamide does not reduce breast or melanoma tumor volume. However, the co-administration of an IDO inhibitor and a chemotherapeutic agent leads to an unexpectedly dramatic reduction in tumor volume. Inasmuch as

1) Hou et al. demonstrate a similar synergy with the use an IDO inhibitor (1MT) and a chemotherapeutic agent as in the instant application and 2) cyclophosphamide has a similar mechanism of action as cisplatin, it is without question that a skilled artisan would find the data provided in Hou et al. dispositive to the issue of whether the co-administration of cisplatin and 1MT would be effective against cancers other than breast cancer, particularly melanoma. Accordingly, it is without question that a skilled artisan is fully enabled to practice the instantly claimed invention for cancers other than breast cancer, particularly melanoma in view of the data provided in Hou et al.

As with Hou et al., the Declaration by Dr. Prendergast under 37 CFR §1.132 (hereinafter Declaration), submitted with the last Official Action response, demonstrates the effectiveness of 1MT (the elected IDO inhibitor species) and the chemotherapeutic agent cyclophosphamide against lung and colon cancers. The Examiner notes that the Declaration shows that "1MT has no effect when administered alone," but incorrectly concludes that this result lends "no support to the efficacy of the instantly claimed treatment against other tumor types." As stated hereinabove, the instant claims are drawn to the co-administration of ***both*** an IDO inhibitor with a chemotherapeutic compound. Further, the instant application demonstrates that the administration of an IDO inhibitor (e.g., 1MT) alone or a chemotherapeutic agent (e.g., cisplatin or cyclophosphamide) alone does not reduce breast tumor volume (see Figure 5). In stark contrast, the instant application demonstrates that the *co*-administration of both 1MT and cisplatin or 1MT and cyclophosphamide led to an unexpectedly dramatic *reduction* in breast tumor volume over a two week course.

The data provided in the Declaration is completely consistent with the data provided in the application. Indeed, the administration 1MT had little to no effect on the lung and colon cancers, the administration of cyclophosphamide slightly

retarded the growth of lung and colon tumors, and the co-administration of 1MT and cyclophosphamide dramatically reduced lung and colon tumor volume. Furthermore, as stated hereinabove, cyclophosphamide and cisplatin are chemotherapeutic agents and both are DNA crosslinkers. Based on 1) a similar mechanism of action of the chemotherapeutic agents used and 2) the same observation that anti-cancer effects are seen only with the ***co***-administration of both the IDO inhibitor (1MT) and the chemotherapeutic agent, a skilled artisan would expect the administration of 1MT and cisplatin (the elected species) would also be effective against lung and colon cancers. Clearly, a skilled artisan would be fully enabled to practice the claimed methods.

In view of the foregoing and the evidence provided in the previous Official Action response, Applicants have demonstrated the effectiveness of the administration of an IDO inhibitor (methyl-TH-DL-Trp, 1-methyl-Trp, and vitamin K3) and a chemotherapeutic agent (cisplatin, paclitaxel, cyclophosphamide, doxorubicin, FTI) against a variety of cancers including melanoma, breast cancer (autochthonous and orthotropic models), colon cancer, and lung cancer. None of the cancers tested have been found to be resistant to the instantly claimed treatment. In light of the broad range of efficacy, Applicants respectfully submit that the instantly claimed methods of treating cancer are fully enabled. Furthermore, any experimentation required of the skilled artisan to practice the instantly claimed methods of treating a cancer in a patient would not be undue in view of the demonstrated effectiveness of the recited compounds against such a wide range of tumors.

Applicants also note that the instant application provides data which demonstrates that the synergistic effect of the administration of an IDO inhibitor and a chemotherapeutic compound occurs with chemotherapeutic compounds which are not DNA crosslinkers. Indeed, Figures 5 and 11 provide data which demonstrates that the synergy is

also seen when chemotherapeutic agents that are DNA intercalators (doxorubicin), farnesyltransferase inhibitors (FTI), and agents that disrupt normal microtubule formation (paclitaxel).

Lastly, Applicants note that the MPEP at §808.01(a) states that a "requirement for restriction is permissible if there is a patentable difference between the species as claimed **and** there would be a serious burden on the examiner if restriction is not required" (emphasis added). Here, the Examiner, as evidenced by the withdrawal of the previous rejection under 35 U.S.C. §103(a), has determined that the instantly claimed methods are free of the prior art. As such, the search burden requirement for restricting among species has been eliminated and Applicants request the Examiner consider additional species, i.e., the other IDO inhibitors and chemotherapeutic compounds recited in the claims. Applicants have provided clear evidence that the genus of chemotherapeutic agents is effective against a panel of caners when co-administered with an IDO inhibitor. Inasmuch as the very reason for requiring a species election has been overcome for the reasons stated above, Applicants respectfully request that the Examiner consider all of the data and evidence previously submitted which clearly demonstrate that the instantly claimed methods are fully enabled.

In view of the foregoing, Applicants respectfully submit that the rejection of claims 38, 39, 41-47, 53, and 54 under 35 U.S.C. §112, first paragraph is untenable and should be withdrawn.

CONCLUSION

In view of the amendments presented herewith and the foregoing remarks, it is respectfully urged that the rejections set forth in the October 15, 2008 Official Action be withdrawn and that this application be passed to issue.

In the event the Examiner is not persuaded as to the allowability of any claim, and it appears that any outstanding

issues may be resolved through a telephone interview, the Examiner is requested to call the undersigned at the phone number given below.

Respectfully submitted,
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